

In the Claims

Please replace all prior versions, and listings, of claims in the application with the following list of claims:

1-91. (Canceled)

92. (Currently Amended) A method for the production of transgenic animals comprising:

a) transfecting a first non-human differentiated somatic cell or cell-line with a transgene construct containing a ~~first~~-DNA sequence;

b) selecting a transfected cell or cell-line into which ~~thesaid first~~ DNA sequence has been inserted into ~~theits~~ genome of ~~said first non-human differentiated somatic cell or cell-line~~, wherein the DNA sequence is operably linked to a promoter;

c) performing a first nuclear transfer procedure to generate a first transgenic animal at least heterozygous for ~~thesaid first~~ DNA sequence, wherein the first transgenic animal and the selected transfected cell or cell-line are of the same species;

d) performing a biopsy or other cell selection technique to obtain cells to establish a second non-human differentiated somatic cell or cell-line from ~~thesaid~~ first transgenic animal;

e) characterizing ~~thesaid~~ second non-human differentiated somatic cell or cell-line ~~using molecular biology methods~~ to ensure that the second non-human differentiated somatic cell or cell-line is at least heterozygous for ~~thesaid first~~-DNA sequence; and

f) performing a second nuclear transfer procedure with at least one ~~one~~-cell of ~~thesaid~~ second non-human differentiated somatic cell or cell-line ~~to produce at least a second transgenic animal at least heterozygous for said first DNA sequence;~~ and,

g) producing ~~a~~the second transgenic animal at least heterozygous for the DNA sequence, wherein the second transgenic animal and the second non-human differentiated somatic cell or cell-line are of the same species.

93. (Currently Amended) The method of claim 92, wherein ~~thesaid~~ first transgenic animal is at an embryonic stage of development.

94. (Currently Amended) The method of claim 92, wherein ~~thesaid~~ first transgenic animal is at a fetal stage of development.

95. (Currently Amended) The method of claim 92, further comprising developing ~~thesaid~~ first transgenic animal into an adult non-human animal.

96. (Currently Amended) The method of claim 92, wherein ~~thesaid~~ first transgenic animal is a mammal.

97. (Currently Amended) The method of claim 92, wherein ~~thesaid~~ first DNA sequence encodes a desired protein.

98. (Currently Amended) The method of claim 92, wherein the genetic composition of ~~thesaid~~ first transgenic animal is characterized to confirm the presence and expression of the DNA sequence~~transgene~~.

99. (Currently Amended) The method of claim 92, wherein ~~thesaid~~ first nuclear transfer procedure further comprises transferring the nucleus of ~~thesaid~~ transfected cell into a suitable enucleated recipient cell of the same species, thereby obtaining a reconstituted cell.

100. (Currently Amended) The method of claim 92, wherein ~~thesaid~~ first transgenic animal is biopsied so as to characterize the genome of ~~thesaid~~ first transgenic animal.

101. (Currently Amended) The method of claim 92, wherein at least one cell from ~~thesaid~~ second non-human differentiated somatic cell or cell-line is expanded through cell culture techniques prior to~~for~~ use in ~~thesaid~~ second round of nuclear transfer so as to allow for the production of ~~produce~~ a multiplicity of animals transgenic for ~~thesaid~~ DNA sequence~~of interest~~.

102. (Currently Amended) The method of claim 96, wherein the source of ~~thesaid~~ differentiated somatic cell or cell-line is an ungulate.

103. (Currently Amended) The method of claim 102, wherein thesaid ungulate is selected from the group consisting of bovine, ovine, porcine, equine, caprine and buffalo.

104. (Currently Amended) A method of preparing a genetically engineered transgenic mammal, comprising:

(a) inseminating a first female non-human mammal recipient with semen from a transgenic non-human animal of the same species ~~known to have~~ that has a transgene present and expressed;

(b) obtaining a transgenic non-human embryo from thesaid first female recipient;

(c) obtaining a differentiated somatic cell from thesaid embryo;

(d) culturing thesaid differentiated somatic cell in a suitable medium, such that a differentiated somatic cell line is obtained; ~~and,~~

(e) performing a nuclear transfer procedure with cells from thesaid differentiated somatic cell line ~~cells~~ to produce at least one transgenic mammal at least heterozygous for thesaid transgene, wherein thesaid transgene encodes a desired gene actuated by a tissue-specific promoter, wherein the transgenic mammal is of the same species as the differentiated somatic cell line; and,

(f) producing the transgenic mammal.

105. (Canceled)

106. (Currently Amended) The method of claim 92, wherein thesaid second non-human differentiated somatic cell or cell-line is obtained from an embryonic goat on or after day 10 of embryogenesis.

107. (Currently Amended) The method of claim 92, wherein thesaid second non-human differentiated somatic cell or cell line is kept in an airtight container.

108. (Currently Amended) The method of claim 92, wherein ~~thesaid~~ first-DNA sequence codes for a biopharmaceutical protein product.

109. (Currently Amended) The method of claim ~~[[108]]~~92, wherein ~~the promoter is asaid~~ first DNA sequence encodes a desired gene that is actuated by at least one beta-casein promoter.

110. (Canceled)

111. (Currently Amended) The method of claim 92, wherein ~~thesaid~~ second non-human differentiated somatic cell or cell-line is obtained from ~~thesaid~~ first transgenic animal by tissue dissociation means including enzymatic means and/or mechanical means.

112. (Currently Amended) The method of claim 92, wherein ~~thesaid~~ second non-human differentiated somatic cell is a fibroblast, cumulus cell, neural cell, mammary cell or a myocyte or ~~thesaid~~ second non-human differentiated somatic cell-line is from a fibroblast, cumulus cell, neural cell, mammary cell or a myocyte.

113. (Canceled)

114. (Currently Amended) The method of claim 104, wherein ~~thesaid~~ transgene codes for a biopharmaceutical protein product.

115. (Currently Amended) The method of claim ~~[[114]]~~104, wherein ~~thesaid~~ tissue-specific promoter is a beta-casein promoter.

116. (Canceled)

117. (Currently Amended) The method of claim 104, wherein ~~thesaid~~ second non-human differentiated somatic cell or cell-line is obtained from ~~thesaid~~ first transgenic animal by tissue dissociation means including enzymatic means and/or mechanical means.

118. (Currently Amended) The method of claim 104, wherein ~~the~~said second non-human differentiated somatic cell is a fibroblast, cumulus cell, neural cell, mammary cell or a myocyte or ~~the~~said second non-human differentiated somatic cell-line is from a fibroblast, cumulus cell, neural cell, mammary cell or a myocyte.

119. (Currently Amended) The method of claim 92, wherein ~~the DNA~~said ~~transgene construct~~ ~~comprises a nucleic acid sequence~~ ~~encodes~~encoding a human polypeptide.

120. (Currently Amended) The method of claim 92, wherein insertion into the genome of the DNA sequence results in~~sa~~id ~~transgene construct is capable of~~ knocking out the expression of a ~~gene~~an endogenous gene of the~~to~~said first transgenic animal.

121. (Currently Amended) The method of claim 119, wherein ~~the DNA sequence~~said ~~transgene construct~~ further comprises a promoter, and wherein the ~~nucleic acid~~DNA sequence is under the control of ~~the~~said promoter.

122. (Currently Amended) The method of claim 121, wherein ~~the~~said promoter is a tissue-specific promoter.

123. (Currently Amended) The method of claim 122, wherein ~~the~~said tissue-specific promoter ~~is a promoter preferentially expressed~~induces expression in mammary gland epithelial cells.

124. (Currently Amended) The method of claim 123, wherein ~~the~~said promoter is selected from the group consisting of a beta-casein promoter, beta-lactoglobulin promoter, whey acid protein promoter and lactalbumin promoter.

125. (Currently Amended) The method of claim 121, wherein ~~the~~said promoter is a caprine promoter.

126. (Currently Amended) The method of claim 119, wherein ~~thesaid nucleic acid encodes a~~ polypeptide is selected from the group consisting of a hormone, an immunoglobulin, a plasma protein, and an enzyme.

127. (Currently Amended) The method of claim 119, wherein ~~thesaid nucleic acid encodes a~~ polypeptide is selected from the group consisting of an alpha-1 proteinase inhibitor, an alkaline phosphatase, an angiogenin, an extracellular superoxide dismutase, a fibrogen, a glucocerebrosidase, a glutamate decarboxylase, a human serum albumin, a myelin basis protein, a proinsulin, a soluble CD4, a lactoferrin, a lactoglobulin, a lysozyme, a lactoalbumin, an erythropoietin, a tissue plasminogen activator, a human growth factor, an antithrombin III, an insulin, a prolactin, and an alpha-1-antitrypsin.

128. (Currently Amended) The method of claim 92, wherein ~~thesaid~~ second non-human differentiated somatic cell is a fibroblast or ~~thesaid~~ second non-human differentiated somatic cell-line is from a fibroblast.

129. (Currently Amended) The method of claim 128, wherein ~~thesaid~~ fibroblast is a primary fibroblast.

130. (Currently Amended) The method of claim 128, wherein ~~thesaid~~ fibroblast is a primary derived fibroblast.